

Comparison of crystal structure and theory for 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP).

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The crystal structure of the food mutagen 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP) has been determined. The monoclinic crystals (P2₁/n) contain two molecules of PhIP and six waters per asymmetric unit. The phenyl groups of the PhIP molecules have different torsion angles with respect to the imidazo-pyridine moiety. The amino groups take part in an extensive hydrogen bond network with the water of crystallization, forming long channels through the crystals. Diffraction results are compared to theoretical calculations of the optimized PhIP geometry in vacuo as well as with water hydrogen bonded to the exocyclic amine. In general, agreement between the x-ray structure of PhIP and its theoretical counterpart is within the combined experimental-theoretical uncertainty. The C-N bond to the exocyclic amine and the neighboring C=N imidazole bond are exceptions. This is attributed to the neglect of the crystal environment, particularly waters of hydration, and the lack of co-planarity between the imidazole ring and the amine group in the calculations. To address the effect of waters of hydration, additional calculations were performed to optimize the geometry with water molecules hydrogen-bonded to PhIP. The resulting C-N exocyclic amine and C=N imidazole geometries were closer to the diffraction results. The accord between theory and experiment demonstrates the utility of applying theory to accurately predict structures of PhIP metabolites and intermediates that are too labile for study by conventional structural techniques. *Work performed under auspices of U.S.D.O.E. at LLNL under contract W-7405-ENG-48, and supported by NIH (CA55861).*